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Anders Per Sorensen

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EXAMINER

MAASHO, KERIMA K

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/563,976	Applicant(s) SORENSEN ET AL.	
	Examiner Kerima Maasho	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 June 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15, 17-24, 29 and 30 is/are pending in the application.
- 4a) Of the above claim(s) 16 and 25-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☒ Claim(s) 12-15, 18 and 19 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>06/05/2006</u> | 6) <input type="checkbox"/> Other: _____ |

Detailed action

Applicant's election made without traverse, of group I drawn to a binding member filed on 06/11/2007, is acknowledged. Election of species of SEQ ID No: 6 and first binding domain was also made without traverse in the reply filed on 06/11/2007. Accordingly claims 16, 25-28 and 31-41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1-41 are pending however only the elected inventions of claims 1-15, 17-24 and 29-30 are under consideration for further examination.

Objection

1. Claims 12-15, 18 and 19 are objected to because of the following informalities: the claims contain non-elected subject matter which must be removed from the claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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2. Claims 12-15, 18, 19, and 22 are objected to because the specification is contradictory regarding what is represented by the elected amino acid of SEQ ID NO: 6. Under sequence listing on page 6, SEQ ID No: 6 refers to CDR4 anti-PsaA 7-1G9 VK, while under complementary-determining regions on pages 18-19 SEQ ID No: 6 refers to CDR3 of amino acid sequence as depicted in Fig 16A. Furthermore, example 6 on page 68 shows that the antibody sequence for 9A7 is depicted in Fig 16 and that antibody 1G9 is depicted in Fig 17. The binding domain of the antibody of the present invention SEQ ID No: 6, does not have a consistent feature in the specification. Does the binding domain for SEQ ID No: comprise CDR3 or CDR4? (see pages 6 and 19 in the specification). Is SEQ ID No: 6 antibody 1G9 or 9A7? (see pages 6 and 919 and example 6 on page 68) Is SEQ ID No: 6 depicted in Fig. 16 or 17?

A 'complete prior art search' could not be done because in the absence of a proper identification of SEQ ID No: 6. Applicants are advised to clarify this matter.

3. Claims 1-15, 17-24 and 29-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-15, 17-24 and 29-30 refer to "an isolated binding member" the claim language used is vague and indefinite. The claims as written relate to any possible product with desirable binding characteristic or property whereas the disclosure provides support for a limited number of such products relating to a polypeptide that can bind to an epitope on a *Streptococcus pneumoniae* protein. While the specification can

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be used to provide definitive support, the claims cannot be read in a vacuum rather, the claim must be definite and complete in and of itself. The claims as they stand are vague and indefinite.

It should be noted that a monoclonal or polyclonal antibody is considered by a skilled person to be a binding member comprising at least one binding domain. Such domain could be variable domain (binding to an antigen) or a constant domain (e.g. binding to an Fc receptor on a cell surface). A polyclonal antibody is considered to comprise a plurality of, mostly monospecific, binding domains. Therefore the claims are treated to mean antibody (monoclonal/polyclonal) in order to facilitate prosecution.

It is suggested that the term "isolated binding member" be changed to "isolated antibody" in order to obviate the rejection.

Claim 10 is vague and indefinite because it is unclear what is encompassed by "N-terminal part". How much of the protein is considered the "N-terminal part"? The metes and bounds of the invention cannot be understood.

Claims 12-15 are vague and indefinite because it is unclear what is considered a 'homologue of SEQ ID NO: 6'. Is this a homologous function or a homologous structure, the two are not necessarily the same. The metes and bounds of the structure encompassed by the term 'homologue' cannot be understood.

Claim Rejections - 35 USC § 112- Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which

it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 12-15, 18 and 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The breadth of the instant claims is drawn to isolated binding members which are not specified in the sequence disclosure. The instant claims read on *any* homologous of any structure or function, as well as homologous with sequences that differ by as much as 40% from SEQ ID NO: 6, e.g., at least 60% homologous. The specification states that substitutions, additions, or deletions may be made to the defined sequences; however, the specification provides no guidance as to what nucleic acids may be changed without causing a detrimental effect to the protein to be produced. Further, it is unpredictable as to which amino acids could be removed and which could be added. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where amino acid substitutions can be made with a reasonable expectation of success are limited. Other positions are critical to the protein's structure/function relationship, e.g., such as various positions or regions directly involved in binding, catalysis in providing the correct three-dimensional spatial orientation of binding and catalytic sites. These regions can tolerate only very little or no substitutions.

The instant claims are drawn to antibodies comprising a sequence with a given percent similarity to a binding domain. Selective point mutation to one key residue could eliminate the function of the polypeptide. It could eliminate its binding properties. If the range of decreased binding ability after single point mutation of a protein antigen varies, one could expect point mutations in the protein antigen to cause varying degrees of loss of function, depending on the relative importance to the binding interaction of the altered residue. Alternatively, the combined effects of multiple changes in an antigenic determinant could again result in loss of function. A protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antibody that precipitously or progressively does not recognize the native antigen in the polyclonal pool. As stated above, Applicants have not shown which amino acids may be changed without causing a detrimental effect to the binding domain in which it represents. The claims allow for as great as 40% variation or even more, e.g., homologues of any function or structure with no recited percent identity to SEQ ID NO: 6. Applicants have provided no guidance to enable one of ordinary skill in the art how to determine, without undue experimentation, the effects of different nucleotide substitutions and the nature and extent of the changes that can be made. It is expensive and time consuming to make amino acid substitutions at more than one position, in a particular region of the protein, in view of the many fold possibilities for change in structure and the uncertainty as to what utility will be possessed. See Mikayama et al. (Nov.1993. Proc.Natl.Acad.Sci. USA, vol. 90: 10056-10060) which teaches that the three-dimensional structure of molecules is important for their biological

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function and even a single amino acid difference may account for markedly different biological activities. Rudinger et al. (June 1976. Peptide Hormones. Biol. Council. pages 5-7) also teaches that amino acids owe their 'significance' to their inclusion in a pattern which is directly involved in recognition by, and binding to, the receptor and the significance of the particular amino acids and sequences for different amino acids cannot be predicted *a priori*, but must be determined from case to case by painstaking experimental study. Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001 clearly states: "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere gem of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." Given the lack of guidance contained in the specification regarding acceptable amino acid substitutions, additions or deletions, one of skill in the art could not make or use the broadly claimed invention without undue experimentation.

Claim Rejections - 35 USC § 112- Written Description

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5. Claims 12-15, 18, 19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth SEQ ID NO:6 and therefore the written description is not commensurate in scope with the claims drawn to homologues or homologs at least 60% identical to SEQ ID NO: 6.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Reiger et al (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlag, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome and differing from other alleles of that locus at one or more mutational sites (page 17). Thus, the structure of naturally occurring allelic sequences are not defined. With the exception of SEQ ID NO: 6, the skilled artisan cannot envision the detailed structure of the encompassed polypeptides and therefore conception is not achieved until reduction

to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The amino acid sequence/protein itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Furthermore, In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

No disclosure, beyond the mere mention of variants is made in the specification. This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore only an isolated antibody comprising the amino acid sequence set forth in SEQ ID NO: 6, but not the full breadth of the claims meets the written description provisions of 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1, 2, 3, 4, 5, 10, 11, 12,-15, 17, 18, 19, 20, 21, 22, and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Korman et al (WO 200114424) in light of Hoogenboom (Trends Biotechnol 1997, vol 15, pp 62-70).

Korman et al teach an isolated binding domain which is 100% identical to Applicant's binding domain set forth in SEQ ID NO: 6. Methods of treatment using said antibody are also disclosed. Although Korman et al do not specifically teach that the isolated antibody is capable of binding *S.pneumoniae* surface adhesion A (PsaA) protein, the structure is identical to that which is claimed so it would inherently possess this function.

Claims 1-15, 17-24, and 29-30 are drawn to a binding member comprising at least one binding domain capable of specifically binding PsaA protein. Wherein, the binding members are selected from antibodies (claims 3, 4, and 23), the binding domain comprises SEQ ID NO:6 (claims 12-15, 18, 19 and 22).

Hoogenboom is merely cited for its teachings whereby the average affinity for antibodies in the naïve primary immune response is shown to be in the range of 10^{-6} to

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10^{-7} , and any higher-affinity antibodies with K_d around 10^{-9} could be designed as required (p 63, right column). For a skilled person in the art the claimed K_d value in the instant invention is considered as an intrinsic value of designing an antigen specific antibody.

7. Claims 1-7, and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Crook et al (Clin Diagn Lab Immunol 1998, filed in the IDS) in light of Hoogenboom (Trends Biotechnol 1997, vol 15, pp 62-70).

Crook et al teach monoclonal antibodies that were produced against PsaA protein and the commonality of PsaA protein and its presence throughout the pneumococcal species by showing reactivity to clinical isolates as well as to the 89 of 90 immunologically distinct serotypes of *S. pneumoniae* (see abstract). The monoclonal antibodies in Crook et al's teaching have at least one portion that recognizes PsaA protein (p 209).

Hoogenboom is merely cited for its teachings whereby the average affinity for antibodies in the naïve primary immune response is shown to be in the range of 10^{-6} to 10^{-7} , and any higher-affinity antibodies with K_d around 10^{-9} could be designed as required (p 63, right column). For a skilled person in the art the claimed K_d value in the instant invention is considered as an intrinsic value of designing an antigen specific antibody.

Therefore Crook et al's teaching meets the limitations of claims 1-7 and 17.

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8. Claims 1-7, 10, and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Srivastava et al (Hybridoma 2000, filed in the IDS) in light of Hoogenboom (Trends Biotechnol 1997, vol 15, pp 62-70).

Srivastava et al disclose mouse monoclonal antibodies that specifically react with PsaA protein and disclose three distinct epitopes on the highly species-specific PsaA protein (abstract). Srivastava et al further teach that the monoclonal antibodies react with the peptide in the N-terminal end of the PsaA protein (p25), and also teach the use of a 15-mer library to imitate the CDR3 regions of the antibodies in this region (p 28, right column). Therefore the above references meet the limitations of claims 1-7, 10 and 22 in the instant invention.

9. Claims 6, 7, 24, 29 and 30 are rejected under 35 U.S.C. 102(b) as anticipated by Gor et al (Infect Immun 2002, vol 70, pp 5589-95) in light of Hoogenboom (Trends Biotechnol 1997, vol 15, pp 62-70).

Claims 6 and 7 refer to a bispecific/multispecific antibody having at least one portion specific towards the PsaA protein. Claims 24, 29 and 30 refer to the binding member comprising two binding domains with one binding domain being specific to PsaA protein.

Gor et al teach the construction of fusion proteins comprising of PsaA linked to cytokine resulting in a peptide with two antigenic determinants. Gor et al teach that such fusion peptide produced PsaA-specific antibodies exclusively of the IgG class and the cytokine retained its characteristic biological activities (abstract and p 5592). Therefore,

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Gor et al's teaching meets the limitations of the binding member being bispecific/multispecific having at least one portion specific towards the PsaA protein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 6-9, 20 and 21 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Srivastava et al (Hybridoma 2000, filed in the IDS) or Korman et al

((WO 200114424) in view of Kriangkum et al (Biomolecular Engineering, 2001, vol 18, pp 31-40) and Hoogenboom (Trends Biotechnol 1997, vol 15, pp 62-70)

Claims 6 and 7 refer to a bispecific/multispecific antibody having at least one portion specific towards the PsaA protein. Claims 8 and 9 refer to the binding domain carried by human and humanized antibody framework. Claims 20 and 21 refer to the variable domains of the heavy and light chains. Claim 23 refer to the antibody fragment selected from Fab, Fab', F(ab)₂ and Fv.

Srivastava et al teach antibodies specific for PsaA peptide and their use as protective immunogenes in mice. Sirivastava also teach that the monoclonal antibodies react with a peptide in the N-terminal end of the PsaA protein. The teachings of Korman et al are set forth above. While Srivastava et al and Korman et al discuss the need to improve the immunogenecity of the peptides with the use of adjuvant (p 29) they do not teach the use of bispecific/multispecific binding members as an enhancement of the immune response to a pneumococcal infection.

Kriangkum et al teach the engineering of bispecific antibodies that uses antibody fragments as building blocks that are made by fusing two different antibodies giving rise to the formation of bispecific antibodies. Kriangkum et al also teach the use of recombinant DNA technology to generate human, chimeric and humanized antibodies as well as antibody fragments such as Fab, Fab', and single chain Fv as well as variable domains of heavy and light chains that are joined together with a linker to form a single polypeptide chain (p 31, left column). While teaching the importance of the use

of bispecific antibodies as therapeutic for the treatment of cancer and infectious disease, Kriangkum does not specifically teach pneumococcal infection.

Hoogenboom teaches the method of protein engineering to generate more human-like (humanized) antibodies as well as the use of transgenic mice expressing human antibodies, wherein the antibodies are created or engineered with their specificity and affinity shaped by the immune system. Hoogenboom also teaches the use of phage antibodies in the generation of fully human monoclonal antibodies by fusing the coding sequence of the antibody variable (V) regions to the amino terminus of the phage. Hoogenboom further teaches that the linkage between antibody genotype and phenotype allows the enrichment of antigen specific phage antibodies using immobilized or labeled antigen. While teaching improved antibody generation in general Hoogenboom does not teach the generation of PsaA-specific antibodies.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve upon the therapeutic ability of the PsaA antibodies taught by Strivastava by generating bispecific/multispecific antibodies as taught by Kriangkum et al for development of single chain variable fragment bifunctional and bispecific antibodies. Humanizing the antibodies as taught by Hoogenboom is also desirable because doing so would give an improved immunogenicity of the PsaA protein with human specificity. Humanized antibodies or chimeric antibodies are a type of monoclonal antibody that have been synthesized using recombinant DNA technology to circumvent the clinical problem of immune response to foreign antigens. The standard procedure of producing monoclonal antibodies yields mouse antibodies. Although

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murine antibodies are very similar to human ones there are differences, and the human immune system recognizes mouse antibodies as foreign, rapidly removing them from circulation and causing systemic inflammatory effects. Accordingly, since streptococcus pneumoniae is one of the leading causes of life-threatening bacterial infection in children and adult humans, responsible for S. pneumoniae meningitis, bacteremia and the most frequent organism isolated from children with otitis media, it would have been obvious to humanize the antibodies taught by Srivastava because doing so would not suffer from the known immune response problems associated with murine monoclonal antibodies, such as systemic and inflammatory effects.

Therefore, there would be a motivation to combine PsaA specific monoclonal antibodies that recognize distinct epitopes of PsaA of Srivastava et al's teaching with Kriangkum et al's teaching to create designer antibody molecules by removing or adding on key protein domains with two or more desired functions through genetic engineering. In addition, combining the above teachings with Hoogenboom's teaching will generate specialized human antibodies through the use of phage-based methods.

By combining the above teachings one skilled in the art would have a reasonable expectation of success. Therefore, the teachings of Srivastava et al, Kriangkum et al, and Hoogenboom are obvious over the above claims of the instant invention because the combined teachings would result in the generation of highly improved PsaA-specific antibodies.

Conclusion

Claims 1-15, 17-24 and 29-30 are rejected for reasons stated above. Claims 12-15, 18, and 19 are further objected to as explained above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kerima Maasho whose telephone number is 571-270-3055. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0906. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer Graser/

Primary Examiner, Art Unit 1645